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Duration and Efficacy of Different Local Anesthetics on the Palmar Digital Nerve Block in Horses

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ABSTRACT

The aim of the present study was to determine the duration and efficacy of three local anesthetics in the palmar digital (PD) nerve block. Nine adult horses were randomly allocated in a crossover design (bupivacaine, 5 mg/mL; lidocaine, 20 mg/mL; and ropivacaine, 7.5 mg/mL). The objective lameness evaluations were recorded before and at 5, 10, 15, 30, 60, 90, 120, 150, 180, 210, 240, and 300 minutes after PD block. The relative lameness severity (RLS) was determined and analyzed using the Tukey–Kramer test ($P < .05$). Lameness improvement (LI) after blocking was determined as a percentage decrease in the quadratic mean (vector sum). The RLS after lameness induction was 4.06 times the threshold (8.5 mm), and the intensity of lameness (time 0) was similar between horses (coefficient of variance = 25%). Five minutes after PD block, all drugs had improved lameness in more than 2.5 times (LI >60%). Bupivacaine, lidocaine, and ropivacaine were effective in blocking at least three times (LI >75%) the experimental lameness. Using 7.5-mg bupivacaine, LI was >3.5 times between 5 and 90 minutes after PD block (LI >83%). With lidocaine (30 mg), between 5 and 90 minutes after blocking a significant LI was observed with a reduction in the lameness intensity greater than 1.2 times (LI >43%). Ropivacaine (11.25 mg) improved lameness in >2.6 times (LI >66%) between 5 and 180 minutes after block. Bupivacaine and ropivacaine showed greater anesthetic effectiveness when compared with lidocaine. The local anesthetics produced a significant LI 5 minutes after blocking. Objective analysis showed a longer analgesic effect of the PD nerve block using ropivacaine than bupivacaine and lidocaine, respectively.

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1. Introduction

Lameness in horses represents the single largest cause of equine morbidity, loss of use, early retirement, and loss of value in their athletic careers [1]. To minimize the losses

associated with lameness, an early and accurate diagnosis allowing for appropriate treatment is essential [2].

Lameness is an indication of a structural or functional disorder in one or more limbs or the back that is evident while the horse is standing or moving, which can be caused by trauma, congenital or acquired anomalies, developmental defects, infection, metabolic disturbances, or any combination of these factors. A complete lameness examination helps to differentiate many types of lameness problems in the horse. The aims of the lameness examinations are to determine whether the horse is lame, which

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limb or limbs are involved, identify the site or sites of the problem, the specific cause of the problem, the appropriate treatment, and the prognosis for recovery. The steps to perform a routine lameness examination include complete history, visual examination of the horse at rest, palpation of the musculoskeletal system, observation of the horse in motion, and manipulative tests such as flexion tests, diagnostic anesthesia, and diagnostic imaging [3].

Local anesthesia is commonly used during a lameness examination to confirm or identify the site or sites of pain where obvious pathology may not exist. Other uses of local anesthesia include providing analgesia during and after surgery and pain control for other painful conditions [3]. The choice of a local anesthetic agent depends mostly on the duration of action the practitioner hopes to achieve [4].

The local anesthetics most frequently used in the United States are 2% lidocaine hydrochloride and 2% mepivacaine hydrochloride. These solutions are potent and rapidly effective but can be locally irritating [3]. Because mepivacaine is longer lasting and less irritating than lidocaine, it is used most frequently. Lidocaine is thought to last only 60 minutes with the maximum effect at 15 minutes [3]. Bidwell et al [5] conducted a study evaluating the duration of mepivacaine in horses with navicular syndrome using a force plate; they observed complete analgesic effect between 15 and 60 minutes after blockade. Schumacher et al [6] observed inefficacy of ketamine as a local anesthetic agent when compared with lidocaine in abaxial nerve block in horses with chronic lameness evaluated with the aid of a body-mounted inertial sensor system. Differently from the studies mentioned previously, several authors have evaluated the efficacy and duration of local anesthetics using the heat-lamp model to observe the loss of cutaneous sensitivity [7–10].

Although mepivacaine is the most frequently local anesthetic used during the lameness examinations, its use can be limited in some countries where the drug is not labeled for horses, such as Brazil. As a result, bupivacaine and lidocaine are used instead during the lameness examination. Through this study, the authors aim to justify the use of these drugs and provide data about a local longer-acting anesthetic—ropivacaine. The objective of the present study was to determine the duration and efficacy of local analgesia produced by bupivacaine, lidocaine, and ropivacaine local anesthetic agents commonly used in equine clinical practice. The information obtained will help to choose the most appropriate drugs in the anesthetic block of horses for lameness diagnosis.

2. Materials and Methods

2.1. Animals and/or Horses

Nine adult horses were selected for this study after a thorough physical examination (subjective evaluation) followed by objective evaluation using a portable wireless sensor-based system by one of the authors. Horse ages ranged between 4 and 15 years (mean, 9.11 ± 3.31 years). Horses' weight ranged between 350 and 513 kg (mean, 449.33 ± 56.72 kg). Based on the objective assessment were included in the study healthy horses with an average

of vector sum (VS) 7.07 ± 1.17 mm (coefficient of variance = 16%) when trotted in hand on loose sand in a straight line.

2.2. Instrumentation

The horses were evaluated objectively using a known system with a set of three wireless inertial sensors (Lameness Locator, Equinosis), prior the application of the hoof clamp, to detect soundness or a minor asymmetry below the threshold value to be included in the study. Then, a baseline lameness severity was determined after the metal clamp was tightened. Horses were taken to trot on a straight line for at least 35 strides (coefficient of variance = 15%), on a flat sand surface. This body-mounted inertial sensor system measures the asymmetry of torso motion before and after performing palmar digital (PD) nerve blocks in horses during the trials. Using this system, the location of lameness to the right or left thoracic limb within the stride is determined by the association of head movement with angular velocity of the right thoracic limb. Maximum (MAXHEADIFF) and minimum (MIN-HEADIFF) head height differences in “mm” between right and left halves of the stride are calculated for each stride, and mean values over all strides are reported. Amplitude of the VS of MAXDIFFHEAD and MINDIFFHEAD correlates with severity of forelimb lameness with a threshold value of 6 mm between lame and sound. The VS was calculated by determining the square root of the sum of the squared values of MAXDIFFHEAD and MINDIFFHEAD [11]. Results of recent studies indicate that this inertial sensor system provides appropriate accuracy and sensitivity for clinical use in equine veterinary medicine, especially for evaluation of horses with mild lameness or for detection of mild improvements in severity of lameness after diagnostic local anesthesia or administration of treatments [12]. A disadvantage of objective lameness evaluation methods that measure asymmetry between right and left limbs is the inability of such methods to reliably detect bilateral lameness [13].

2.3. Lameness Induction

Before the beginning of the experiment, horses had their routine farrier work done including balanced trimming and the placement of shoes in the forelimbs to prevent distal migration of the metal clamps. The model of experimental lameness used was a modification of that previously described by Swaab [2], to limit the hoof expansion by putting pressure on the hoof wall, resulting in noticeable reversible lameness, simulating lameness caused by a tight shoe. Galvanized steel clamps (Fig. 1A) were used, one at a time, to induce lameness. The width of the clamp at the heels was reduced by approximately 50% to prevent impingement on the heel bulbs or coronary band. To prevent slippage when tightened, the clamp was secured to the hoof wall by two metal plates and two screws fixed on the dorsolateral and dorsomedial aspect of the hoof wall (Fig. 1B). The large screw, to tighten the metal clamp, was directed laterally in all cases to avoid trauma during pressure adjustment (Fig. 1C). The pressure of the steel clamp was gradually increased until horses showed

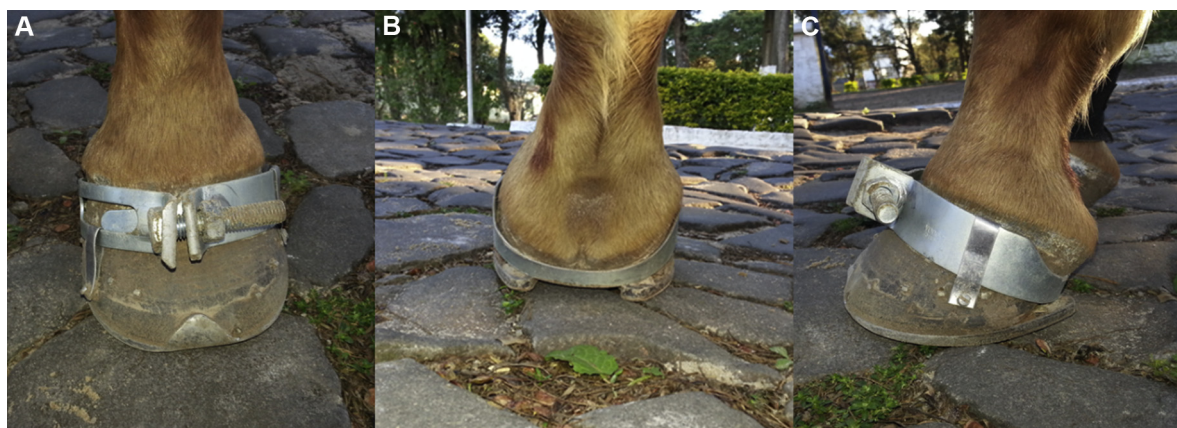


Fig. 1. (A) Galvanized steel clamps were used to induce lameness by limiting the expansion and putting pressure on the hoof wall, resulting in noticeable reversible lameness. (B) The width of the palmar portion of the clamps was reduced by approximately 50% to prevent impingement on the heel bulbs or coronary band. (C) To prevent slippage when tightened, the clamp was secured to the hoof wall by two metal plates, and two screws were fixed on the dorsolateral and dorsomedial aspect of the hoof wall to secure the metal plates. The screws were directed laterally in all cases to avoid trauma to the sensitive lamina during pressure adjustment.

lameness grade III according to the American Association of Equine Practitioners (AAEP) scale I to V [14], when evaluated subjectively, and values of VS between 22 to 53 (mean, 34.05 ± 8.74) in the objective analysis. In horses that had a subtle lameness, the sound limb was preferentially used for lameness induction to minimize potential interference. Lameness was induced only on the forelimbs. After the return of lameness (end of blocking effect) or after 300 minutes of experiment, the clamps were removed, being replaced before the next treatment.

2.4. Experimental Design

Using a crossover design, all horses were alternately treated with three commercially available local anesthetics: 2% lidocaine (20 mg/mL), 0.5% bupivacaine (5 mg/mL), and 0.75% ropivacaine (7.5 mg/mL) after being experimentally subjected to foot pain to produce AAEP grade III lameness. The order of treatments was randomly assigned. A washout period between treatments was at least 24 hours. Preparation of the skin for the nerve block was limited to a brief scrubbing the nonclipped skin with 70% alcohol. The PD nerve block was performed by injecting 1.5 mL of local anesthetic with a 26-G needle (13×0.45 mm) subcutaneously just palmar to the medial and lateral neurovascular bundles and just proximal to the collateral cartilages of the foot. The same clinician performed the nerve blocks and evaluations on all patients. Between 5 and 30 minutes after the administration of the anesthetic, the effectiveness of the nerve block was checked by applying pressure with a pointed object over the heel bulbs. The contralateral digit was also tested in the same manner to verify whether the horse would react when pressure was applied to the nonblocked skin. Both absence of response to stimulation of the skin in the blocked digit and lameness improvement (LI) were required to consider a block effective. Lameness evaluation was performed immediately before administration of the anesthetic and 5, 10, 15, 30, 60, 90, 120, 150, 180, 210, 240,

and 300 minutes after the block. Thirty minutes after the hoof clamp was removed, at the end of the trials (after the return of lameness or after 300 minutes of experiment), the animals were again evaluated to assess whether there was any residual lameness caused by the clamps.

2.5. Statistic Analysis

Data collected with the portable inertial system-based sensors (Lameness Locator) were analyzed with a dedicated software, and the results were interpreted according to recommendations made by the manufacturer. The quadratic mean (VS) of meanMINDIFFhead and meanMAXDIFFhead was used as the indicator of lameness severity, whereas the sign of meanMINDIFFhead determined the affected limb: positive sign, right front; negative sign, left front. The VS is an estimate of the amount of vertical head movement asymmetry; this has higher precision for lameness detection [13]. The threshold of 8.5 mm was recommended by the manufacturer. The coefficients of variation of MINDIFFhead (standard deviation of MINDIFFhead/meanMINDIFFhead) and MAXDIFFhead (standard deviation of MAXDIFFhead/meanMAXDIFFhead) were used as indicators of variability. For each time point, a relative lameness severity (RLS) was calculated as measured lameness severity/threshold. For each time point after lameness induction, a relative change in lameness severity was calculated as $RLS_{\text{timepoint}}/RLS_{\text{induced}}$. The Kolmogorov-Smirnov test and the White test were used to analyse the lameness severity. Finally, we used analysis of variance for repeated data (multiple comparison test) followed by confirmatory test (Tukey–Kramer) (unbalanced data). Significant improvement was considered if $P < .05$. Amplitude of LI after blocking was determined as a percentage decrease in VS from baseline evaluation (before block) or $[(VS \text{ before block} - VS \text{ after block}) / (VS \text{ before block} - VS \text{ threshold})]$. The LI% of horses was analyzed over time, as well as the standard deviation for each time.

2.6. Approval by the Animal Care and Use Committee

The Federal University of Santa Maria Research Committee of Ethics on Animal use approved this study (Protocol 23081.015650/2013-25).

3. Results

Right after tightening the clamps, a noticeable lameness was consistently achieved and maintained, comparable with a subjective evaluation grade III/V lameness. The modified protocol chosen to induce experimental lameness demonstrated to be uncomplicated and very reliable as previously documented by Swaab [2]. No injuries or residual lameness were noted after the clamp removal or at the following data collection 30 minutes after. Thus, the experimental model used in this study was considered to be adequate to study hoof lameness in horses.

Fig. 2 contains the relative change in lameness severity after PD nerve block with lidocaine, bupivacaine, and ropivacaine as from 5 minutes after injection. The LI assessment is presented as % of LI (Fig. 3).

The RLS observed after the induction of lameness (time 0) was 4.06 ± 1.01 times the threshold (8.5 mm), and the intensity of the induced lameness was similar between horses (coefficient of variance = 25%). Five minutes after the PD block, all tested drugs had improved lameness in more than 2.5 times (LI >60%). Bupivacaine, lidocaine, and ropivacaine were effective in blocking at least three times (LI >75%) lameness induced by clamps.

The use of 7.5 mg of bupivacaine per nerve branch improved lameness in 6.8 ± 4.88 times the severity of lameness induced (LI = 98%) at 30 minutes after the PD block. Between 5 and 90 minutes, LI was higher than 3.5 times (LI >83%). From 120 minutes on, there was a progressive decrease in the analgesic action of bupivacaine and horses returned to show mild lameness.

With 30-mg lidocaine per nerve branch, maximal analgesia was obtained at 30 minutes when the induced lameness improved by 3 times ± 1.62 (LI = 77%). Between 5 and 90 minutes after blocking, there was a significant improvement in lameness with a decrease of more than 1.2 times the induced lameness (LI >43%), however, from 90 minutes to a decrease in analgesia. Only one horse of this group remained lameness-free after 210 minutes.

Administration of 11.25 mg of ropivacaine per nerve branch was able to improve lameness in 6.7 ± 5.04 times at 150 minutes after blocking (LI = 95%). As of 5 minutes and up to 180 minutes, the LI was higher than 2.6 times the induced lameness (LI >66%). However, after 210 minutes, analgesia decreased.

There was no loss in skin sensitivity in five horses (5 of 9) blocked with lidocaine within 30 minutes after the block; in those animals treated with bupivacaine, only one horse (1 of 9) did not present loss of skin sensitivity by up to 30 minutes after administration of the drug; in horses blocked with ropivacaine, all animals did not present skin sensitivity during the trials.

4. Discussion

The horses used in this study were clinically healthy (free of lameness) or had imperceptible lameness with an average value of 7.07 ± 1.17 mm VS. All horses tolerated the placement of the clamps. Hoof wall or coronary band lesions were not observed in any limb treated up to 300 minutes of experiment. The results of this study reproduced those observed by Swaab [2], which also induced reversible clinical lameness with steel clamps around the heels establishing lameness grade II according to AAEP standards [14] assessed by experienced evaluators, and using an objective evaluation by a force plate. This method of lameness induction yields a reversible lameness in horses and does not result in complications.

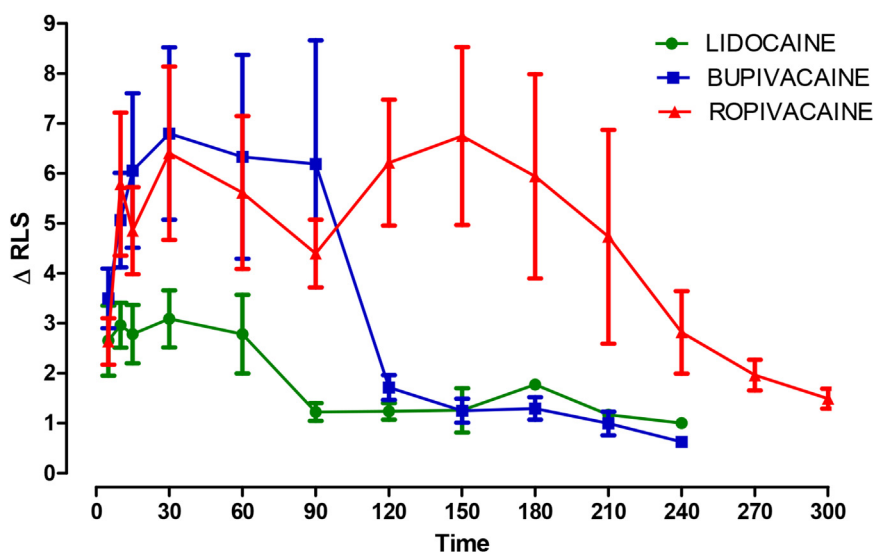


Fig. 2. Graphics of relative change in lameness severity (y axis) over the time (x axis) after a palmar digital nerve block with 1.5 cc of lidocaine, bupivacaine, and ropivacaine. RLS, Relative lameness severity.

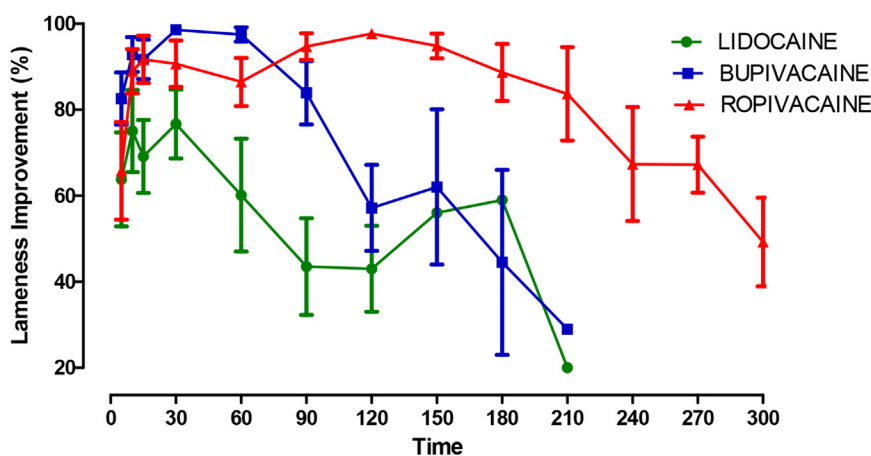


Fig. 3. Graphics of lameness improvement in percentage (y axis) over the time (x axis) after a palmar digital nerve block with 1.5 cc of lidocaine, bupivacaine, and ropivacaine.

Rungsri et al [15] showed that the improvement of lameness after a distal interphalangeal joint block was greater after 5 and 10 minutes than after 2 minutes of intraarticular injection of 5 mL of mepivacaine. Considering the finding of Rungsri et al, the analysis started at 5 minutes after PD block because local anesthetics would have better distribution and early clinical significant effect. Even in different doses and at different concentrations, all drugs were effective in blocking at least three times of the lameness induced by the metal clamps ($LI > 75\%$); 5 minutes after blocking, the tested drugs have improved lameness more than 2.5 times ($LI > 60\%$). Greater anesthetic effectiveness was observed of bupivacaine and ropivacaine when compared with lidocaine, as bupivacaine and ropivacaine were able to improve up to 6.8 ($LI = 98\%$) times the lameness induced compared with lidocaine only for three times ($LI = 77\%$).

Between 5 and 90 minutes after the administration of 7.5-mg bupivacaine at each branch of the PD nerves, there was a significant clinical improvement in lameness. Testing skin sensitivity through heat-projection lamp model by Harkins et al [8] obtained significant analgesia 7.5 minutes after an abaxial sesamoid nerve block with 2 mg of bupivacaine. The analgesic effect was observed 15 minutes after administration of 0.5 to 1 mg of bupivacaine. Local analgesia remained significant 45 minutes after administration of 0.5 mg and 90 minutes after the administration of 1 and 2 mg of bupivacaine. Even using a higher dose of bupivacaine than used in Harkins et al [8] studies, it was evidenced that similar duration of analgesia, suggesting that as of 2 mg bupivacaine per site, has a dose-dependent effect.

Taking into account the fact that the volume of the drug may interfere with the specificity of the block, by blocking unwanted structures when using higher volumes, is interesting to make the block with the smallest amount of anesthetic capable of producing analgesia.

A difference was observed between 5 and 90 minutes after block with lidocaine, but clinically it was observed that there was a progressive return of lameness from 60 minutes. Maximal analgesia with 30-mg lidocaine was obtained at 30 minutes when the lameness improved by 3 ± 1.62 times

($LI = 77\%$). As lidocaine provides analgesia for a short period, its use is most suitable in animals with only one source of pain [3]. Harkins et al [9] evaluated the skin sensitivity after exposure to a heat-projection lamp observed a significant anesthetic effect of PD nerves performed at the sesamoid bones with 10 and 40 mg of lidocaine, 15 minutes after administration. Analgesia persisted for 30 and 90 minutes, respectively. Evaluating the skin sensitivity, Spoormakers et al [10] evaluated the anesthetic potency, onset, duration, and side effects of lidocaine and lidocaine associated with epinephrine in blocking the nerves on the lateral and medial palmar aspect of the proximal metacarpus. In that study, 10 mL of 2% lidocaine were injected by the nerve branch, and skin sensitivity was the variable to measure the anesthetic effect. The onset of anesthesia occurred 5 to 15 minutes after treatment in both groups. In the group treated with lidocaine without epinephrine, the effect lasted 60 minutes, and the maximum effect was observed in 15 minutes. In the group treated with lidocaine associated with epinephrine, moderate or total effect lasted 6 hours in most animals, reaching 9 hours in two animals, with a maximum effect at 60 and 90 minutes. Comparing the results with Harkins et al [9] and Spoormakers et al [10], similar duration of analgesia with 30, 40, and 200 mg of lidocaine per site was observed in this study, suggesting that the drug has one dose-dependent effect as of 30 mg. To use the lowest dose capable of producing analgesia, it should be noted that the dose of 30 mg of lidocaine was able to revert in 77% of the experimental lameness at 30 minutes, and perhaps a higher dose would be necessary to produce more consistent clinical outcome.

The dose of 30 mg of lidocaine was able to improve lameness in only 77%; this is consistent with what has been previously reported in another studies [15,16] used for determination of unequivocal decrease in severity of lameness after blocking a cutoff value of 70% improvement in the objective lameness parameter of VS of HDmax and HDmin.

An injection of 1.5 mL of ropivacaine (11.25 mg) in the PD block resulted in a significant LI higher than 66% the baseline after 5 minutes. Harkins et al [7] obtained analgesia 7.5 minutes after injection of 1 and 4 mg of

ropivacaine in the abaxial side block with the effect remained for 30 and 150 minutes, respectively. Santos et al [17] found that 40 mg of intraarticular ropivacaine produced analgesia with onset of action within 30 minutes in horses with lipopolysaccharide-induced synovitis in the radiocarpal joint, and the clinical analgesia lasted between 150 and 210 minutes in the inflamed tissue. The duration of analgesia observed in this study was longer than Harkins et al [7] results with a lower dose. However, comparing to Santos et al [17] results, who used the higher dose but via intraarticular, the duration of analgesia was longer than observed in this study with a PD block.

In the present study, no side effects were seen after administration of the three anesthetic agents tested separately in the PD nerve block, perhaps because of the small volume that was injected subcutaneously. Spoomakers et al [10] reported swelling as the main side effect that occurred within 2 days after the administration of 10-mL lidocaine 2% and 10-mL lidocaine 2% with 10-mcg/mL epinephrine in blocking the palmar nerves at the proximal aspect of the metacarpus.

Despite of the significant improvement in the experimental lameness, there was no loss of local skin sensation in five (5 of 9) horses blocked with lidocaine within 30 minutes after the block. In those treated with bupivacaine, only one horse (1 of 9) did not present loss of skin sensation by up to 30 minutes after administration of the drug. In horses blocked with ropivacaine, all animals had no local skin sensation. Perhaps the lidocaine dose used was insufficient to cause complete desensitization skin.

In the routine lameness examination, clinicians test the skin for sensitivity as to determine if a nerve block has been achieved. Although many studies have used the skin sensation as the criteria to assess anesthetic nerve block effectiveness, Schumacher et al [18], based on their clinical experience, believe that despite of loss of skin sensation at the coronary band after a PD nerve block, analgesia of other structures in the foot may be incomplete. Some horses may retain cutaneous sensation after lameness has been ameliorated by anesthesia of the PD nerves. On the other hand, some horses can maintain skin sensitivity after the blockade even with resolution of lameness.

Anesthetic drugs of different concentrations were chosen for this experiment based on their frequent use in lameness examinations and postoperative analgesia; moreover, the easy access to these drugs for clinicians was also considered. The concentration of lidocaine and bupivacaine used was the same one used by Harkins et al [8,9] and Spoomakers et al [10]. The concentration of ropivacaine was less than that used by Santos et al [17] and greater than that used by Harkins et al [7]. The dose and concentration of the drugs can influence the timing of beginning and ending of the anesthetic action, explaining the differences in time of action found by different authors [7–10,17].

Although Bidwell et al [5] had evaluated the duration of the analgesic effect of mepivacaine with a force plate, the authors are unaware of the existence of studies that objectively evaluated the potency, efficacy, and duration of the drugs tested in this study. In the same way, there are not many studies assessing the potency of these drugs by

comparing the relative change in lameness severity. Through this study, we sought to assess the duration of analgesia with bupivacaine, lidocaine, and ropivacaine on the resolution of the experimental lameness, whereas previous studies valued the moment of loss of the cutaneous sensitivity. Harkins et al studies assessed the anesthetic effect of bupivacaine, lidocaine, and ropivacaine using the heat-projection lamp and limb withdrawal reflex as the experimental model, and Spoomakers et al study evaluated the skin sensitivity tested by touching the skin at a pre-determined site with a stick with a blunt nail on the end, to elicit withdrawal of the leg, none evaluated LI [7–10]. In some cases, loss of skin sensitivity was not observed, although there was improvement in lameness. This may explain the differences observed between studies that evaluated the anesthetic response on lameness resolution and those that were based on loss of skin sensitivity.

Ropivacaine is recommended for procedures that require long analgesic duration, as lameness examination with pain originating from different limbs or for orthopedic surgery recoveries. Bupivacaine showed duration on analgesic effects as reported in the literature. Lidocaine provides a short-term analgesic effect; therefore, it is more appropriate for procedures that require brief analgesic effect as examination of mixed lameness on the same limb.

5. Conclusions

Bupivacaine and ropivacaine showed greater anesthetic potency when compared with lidocaine. Five minutes after PD block, all local anesthetics showed significant improvement in lameness, suggesting that some degree of anesthesia might have been obtained even earlier. Objective analysis of LI showed a longer analgesic effect using ropivacaine than bupivacaine or lidocaine on the PD nerve block.

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